## REMARKS

As an initial matter, Applicants note that the pending claims have been re-numbered as required by the Examiner. Claims 1-47 are now pending in this application. Claims 9, 17-21, 23, 33, 34, and 44 have been elected with traverse for prosecution in the present application. Claims 9, 17-21, and 23-47 are currently amended. Claims 1-8, 10-16, 22, 24-32, 35-43, and 45-47 have been withdrawn. For the reasons detailed below, Applicants respectfully request rejoinder of claims 1, 3, 5-8, 13, and 43.

### Traversal of Restriction Requirement

The Office has divided the claims into twenty-four independent and distinct inventions, and requires that Applicants elect one invention for prosecution in the present application. Applicants respectfully traverse this restriction requirement as it is applied to Groups I (claims 1, 5-8, 33, 34, and 43), III (claims 3, 5-8, and 43), V (claims 9, 17-21, 23, 33, 34, and 44), and IX (claims 13, 17-21, and 44).

The claims of Groups I, III, V, and IX are directed to diagnostic methods for determining the presence or severity of a disease affecting a joint that require determining OP-1 protein levels in patient tissue samples. Where inventions are related, as they are in the present application, the Office *must* show that the restriction is proper. The M.P.E.P. states:

> Where . . . the classification is the same and the field of search is the same and there is no clear indication of separate future classification and field of search, *no reasons exist for dividing among related inventions*. M.P.E.P. § 808.02 (Emphasis added)

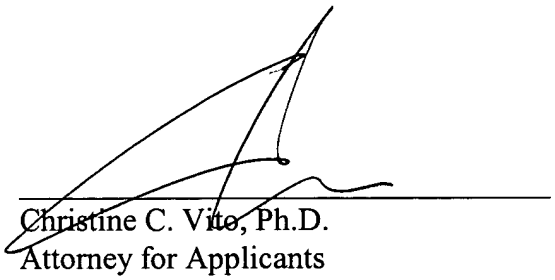
It is improper to divide related inventions unless they belong to different classifications or require searching different fields. In the present case, Groups I, III, V, and IX all belong to class 435, as indicated at pages 2 and 3 of the Office Action mailed on September 30, 2004. Different fields of search are not required because all of these groups require analyzing OP-1 protein level. On this basis alone, the restriction requirement as it applies to Groups I, III, V, and IX should be withdrawn.

The Office is concerned that the inventions defined by the various groups are incapable of use together, and that the claimed methods have different effects in different patient populations. These concerns, as they apply to the inventions of Groups I, III, V, and IX, are misplaced. The claimed methods are based on Applicants' discovery that OP-1 protein levels are highest in healthy joints and are reduced in joint tissue as a function of age or inflammation (page 11, lines 19 and 20). Applicants' discovery provides for the use of OP-1 protein level as a biomarker that indicates the presence or severity of a joint disease in a patient, where the disease is characterized by cartilage tissue deterioration (page 15, line 26, to page 16, line 18). Given that a single biomarker is used to distinguish among joint diseases that share a common clinical feature, i.e., cartilage deterioration, the claimed diagnostic methods are clearly capable of use together and do not have different effects in different patient populations. In sum, the invention of Groups I, III, V, and IX are related, belong to the same class, and are capable of search together. Reconsideration of the restriction requirement is respectfully requested.

## CONCLUSION

The Examiner is invited to contact the undersigned to discuss any outstanding issues. Early favorable action is respectfully requested.

Respectfully submitted,



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